



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0315]

E2C(R2) Periodic Benefit-Risk Evaluation Report and E2C(R2) Periodic Benefit-Risk Evaluation Report--Questions and Answers; International Council for Harmonisation; Guidances for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of guidances for industry entitled "E2C(R2) Periodic Benefit-Risk Evaluation" (E2C(R2) guidance) and "E2C(R2) Periodic Benefit-Risk Evaluation Report--Questions and Answers" (E2C(R2) Q&A guidance). These guidances were prepared under the auspices of the International Council for Harmonisation (ICH), formerly the International Conference on Harmonisation. The E2C(R2) draft guidance, issued April 11, 2012, updated and combined two ICH guidances, "E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs" (E2C guidance) and "Addendum to E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs" (addendum to the E2C guidance). The E2C(R2) guidance is intended to describe the format, content, and timing of a Periodic Benefit-Risk Evaluation Report (PBRER) for an approved drug or biologic, and it finalizes the draft guidance. The E2C(R2) Q&A guidance is a supplementary guidance that is intended to clarify key issues in the E2C(R2) guidance.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked, and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2012-D-0315 for "E2C(R2) Periodic Benefit-Risk Evaluation Report and E2C(R2) Periodic Benefit-Risk Evaluation Report--Questions and Answers; International Council for Harmonisation; Guidances for Industry; Availability." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR

56469, September 18, 2015, or access the information at:

<http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of these guidances to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002, or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. The guidances may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance documents.

FOR FURTHER INFORMATION CONTACT: Regarding the guidance: Maureen Melvin, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4480, Silver Spring, MD 20993-0002, 301-796-5366; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

Regarding the ICH: Amanda Roache, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 1128, Silver Spring, MD 20993-0002, 301-796-4548.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products for human use among regulators around the world. The six founding members of the ICH are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; CDER and CBER, FDA; and the Pharmaceutical Research and Manufacturers of America. The Standing Members of the ICH Association include Health Canada and Swissmedic. Any party eligible as a Member in accordance with the ICH Articles of Association can apply for membership in writing to the ICH Secretariat. The ICH Secretariat, which coordinates the preparation of

documentation, operates as an international nonprofit organization and is funded by the Members of the ICH Association.

The ICH Assembly is the overarching body of the Association and includes representatives from each of the ICH members and observers.

In the Federal Register of April 11, 2012 (77 FR 21782), FDA published a notice announcing the availability of a draft guidance entitled "E2C(R2) Periodic Benefit-Risk Evaluation Report." The draft E2C(R2) guidance updated and combined the E2C guidance and the addendum to the E2C guidance. The notice gave interested persons an opportunity to submit comments by May 11, 2012.

After consideration of the comments received and revisions to the guidance, a final draft of the guidance was submitted to the ICH Steering Committee and endorsed by the regulatory agencies in November 2012.

The E2C(R2) guidance provides guidance on the format, content, and timing of a PBRER for an approved drug or biologic, and it finalizes the draft guidance. The PBRER will serve as a common standard for periodic reporting on approved drugs or biologics among the ICH regions. The harmonized PBRER is intended to promote a consistent approach to periodic postmarket safety reporting among the ICH regions and to enhance efficiency by reducing the number of reports generated for submission to the regulatory authorities.

Since the E2C(R2) draft guidance was made available in 2012, ICH has identified questions linked to the interpretation and application of the E2C(R2) guidance. The E2C(R2) Q&A guidance is intended to clarify questions relating to implementation of the E2C(R2) guidance.

These guidances are being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidances represent the current thinking of FDA on the E2C(R2) PBRER. They do not establish any rights for any person and are not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

These guidances refer to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520). The collection of information in the "Guidance on Reporting in Accordance with International Council for Harmonisation--Periodic Benefit-Risk Evaluation Report (E2C(R2)) and Providing Waiver-Related Materials" has been approved under OMB control number 0910-0771. The guidances also reference other collections of information. The collection of information in 21 CFR 314.80 has been approved under OMB control number 0910-0230, and the collection of information in 21 CFR 600.80 has been approved under OMB control number 0910-0308.

III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.regulations.gov>,
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>,
or
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

Dated: July 13, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-17009 Filed: 7/18/2016 8:45 am; Publication Date: 7/19/2016]